



*[Handwritten signature]*

**NOVTRAN cDNA sequence:**

atgcagtggtcctgtctggcctgtacctcctcagggtcctcccatgtcctgtctctcctgagagaccctgtgcctgtgccacagggaaccaagctcttc  
cactcctgtatcacctcaacgaacccatgcgcctcctcctggaggttgcctgtgaagctgcaggcatcacccctggagctagggctctgagcacccgac  
ctgtccatattccatccctgcctcctcctgtccacgactcctcaacagaccatccctgtcctctcaacaggcccccgtctgtctgggaacca  
cggacagaggccttcccatcccaggcctgaaggccagagtgggtgggaacatcctcgccgaagccggcctcaattctcaaggccatgcctggagc  
cagtgccatctggaccctctgggtcaagcaagggtgtgtctaatcaaggcaggccctcgaggatgccaaaggcccggaatgccagtggaacg  
tgaaaaccttctgtgacaaacctgcagtgccctctctgtctccagctgtctccagctctccatgcacaaagggaacagagcaggagcagtaatg  
cgggaatttgacttgcaagtcggggcgtcgggattacaattcaaggctgtgtgaaactcgggcagatccagctgcaaaaggcagttccttctcga  
gctgcagaacgtgtctggaggggttggtcagcccgaggtcccaggaaccactgcaaggtggggcgggcctcagagcccttcccagagctggg  
ggctggtagccccccttggcttggagaaggtcagtaaccaaccattcccaggcccgactcggaagggtgtggaactggccccctgtgtcctcgt  
gaccagtgctccactgtgcactctcccaggccagccgaacctggcacacactgggtgttccctaaatagccatggagggtattgtggcatggagagctgtc  
gattccagaacctcctggacatagggtgggagctcatctgcagaagctgctga (SEQ ID NO: 1)

**Fig. 1A**

**NOVTRAN Protein Sequence:**

MQWSCLACTLLRVLPHVLSLLRDPVPVPTGTLFHSCITSTNPFCASFLVAVEAAGITPW  
TVGSEHPPCPYPSLHASFFTDSEFNRPSPAPLNRPRSAGEPRTEAFSPGLKARVGGTILAE  
AGLNSQGHAVEPVPSPGSGSSKGCVLIGRPSRMPKARECPVDRENLLLTNPVAVPSLLQL  
LSSSPCIKVETEQRSEAEFDLQSRARDYNSRLLKLGQIPAAKGSSFLELQNVSGGVG  
SARGPRNHCKVGAGPQSPFPELGAGSPPLALEKVSTQPIPQARLRKGVDPVPSPGDQC  
PLCTLPGQPNLAHTGCSLSNHGGYCGMESCRFQKPPGHRAGSSSAEAA (SEQ ID NO: 2)

**Fig. 1B**

09730617-070901



BlastN for NOVTRAN:  
gb:GENBANK-ID:H55724|acc:H55724 CHR220663 Chromosome 22 exon Homo sapiens  
genomic clone C22\_916 5', mRNA sequence - Homo sapiens, 171 bp.

Minus Strand HSPs:

Score = 585 (87.8 bits), Expect = 1.0e-19, P = 1.0e-19  
Identities = 117/117 (100%), Positives = 117/117 (100%), Strand = Minus /  
Plus  
Query: 735 ACCTCGGGCTGAGCCAACCCCTCCAGACAGTTCTGCAGCTCGAGGAAGGAAGTCCCTT 676  
|||||  
Sbjct: 18 ACCTCGGGCTGAGCCAACCCCTCCAGACAGTTCTGCAGCTCGAGGAAGGAAGTCCCTT 77  
  
Query: 675 TGCAGCTGGGATCTGCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 619 (SEQ ID NO: 19)  
|||||  
Sbjct: 78 TGCAGCTGGGATCTGCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 134 (SEQ ID NO: 20)

Fig. 2A

09730617-076901



# BlastX for NOVTRAN:

NoHits:

ptnr:SWISSPROT-ACC:P22357 ANOTHER-SPECIFIC PROTEIN SF18...	-3	102	0.0093	1
ptnr:SPTREMBL-ACC:Q26876 PROTECTIVE RECOMBINANT ANTIGE...	-3	87	0.018	1
ptnr:TREMBLNEW-ACC:AAD41775 PRO-ALPHA-2(I) COLLAGEN - ...	-3	86	0.061	2
ptnr:PIR-ID:S46272 anther-specific protein - common su...	-3	94	0.073	1
ptnr:SPTREMBL-ACC:Q26874 PROTECTIVE RECOMBINANT ANTIGE...	-3	78	0.16	1
ptnr:SPTREMBL-ACC:Q92029 ALPHA-1 COLLAGEN TYPE III - G...	-3	86	0.19	3
ptnr:SWISSPROT-ACC:P46804 SPIDROIN 2 (DRAGLINE SILK FI...	-3	101	0.24	1
ptnr:SPTREMBL-ACC:Q57808 103AA LONG HYPOTHETICAL PROTE...	+2	76	0.25	1
ptnr:SWISSNEW-ACC:P41484 PROLINE-RICH ANTIGEN (36 KD A...	-3	95	0.26	1

## CuraBLASTX Analysis of AC007663\_A

PUBLIC DATABASE

Query= AC007663\_A Cura\_109 transmembrane protein  
(1047 letters)

Database: /opt/database/public/blast/ptnr  
577,633 sequences; 178,813,065 total letters.

Sequences producing High-scoring Segment Pairs:	Smallest Reading Frame	High Score	Sum Probability	
			P(N)	N
ptnr:SWISSPROT-ACC:P22357 ANOTHER-SPECIFIC PROTEIN SF18	-3	102	0.015	1
ptnr:pir-id:S12246 anther-specific protein SF18 precur	-3	102	0.015	1

PATENT DATABASE

## CuraBLASTX Analysis of AC007663\_A

Query= AC007663\_A Cura\_109 transmembrane protein  
(1047 letters) of query sequence in all 6 reading frames

Database: /opt/database/licensed/blast/geneseq\_aa  
349,121 sequences; 51,277,408 total letters.

Sequences producing High-scoring Segment Pairs:	Smallest Reading Frame	High Score	Sum Probability	
			P(N)	N
patp:R28916 Type III procollagen (prior art) - Homo sa...	+1	81	0.059	3
patp:W03454 Mutant mouse c-AKT non-translation region ...	+1	81	0.075	1
patp:G04146 Arabidopsis thaliana protein fragment SEQ ...	-3	80	0.095	1

Fig. 2B

09730617-070901



09730617-070001

**NOVNEUR cDNA sequence:**

Regions 135319 to 135129 (1-190bp) and 134487 to 134314 (191 to 364bp) of the genomic clone (in - frame). Further extended using ESTs AI739078, AI767488, and AI796217.

AGCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGCATGGCCCGCGGCGGGAGGGCGCTCGGATGTTTCGGC  
AGCCTCCTGCACTTCGCCCTGCTCGCTGCCGCGCTCGTCCCGCTCAGCTGGGATCTCCCGAGCCCCGCA  
GCCGAGCCAGCAAGATCCGAGTGCACTCGCGAGGCAAGCTCTGGGCCATCGGTCACCTTCATGGGCAAGAA  
GAGTCTGGAGCCTTCCAGCCCATCCCATTTGGGGACAGCTCCCCACACCTCCCTGAGGGACCAGCGACTG  
CAGCTGAGTCATGATCTGCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCG  
CACCCCAATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATGGGGCAGACA  
CAACAGCGTGGCTTAGATTGTGCCCAACCAGGGAAGGTGCTGAATGGGACCTGTTGATGGCCCCATCTG  
GATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATTTCTGGCTGGGTCAACAGAAATATC  
GCTGATGCAGACAGATTATGTTCTGCTGATTTCCTGCTCCCTGTTGAATTGGTGAATAAAACCTT  
GCTCTATACATACAAA (SEQ ID NO: 3)

**Fig. 3A**

**NOVNEUR Protein sequence:**

MFGSLHLHFALLAAGVVLPSWDLPEPRSRASKIRVHSRGKLWAIGHFMGKKSLPSSPSPLGTAPHTSLRDQRLQLSH  
DLLGILLKKALGVSLSRPAPQIQYRRLVQILQK (SEQ ID NO: 4)

**Fig. 3B**



**BlastN for NOVNEUR:**

gb:GENBANK-ID:HUMNBK|acc:M21551 Human neuromedin B mRNA, complete cds -  
Homo sapiens, 640 bp (RNA).

Top Previous Match Next Match

Length = 640

**Plus Strand HSPs:**

Score = 3055 (458.4 bits), Expect = 9.1e-132, P = 9.1e-132

Identities = 629/639 (98%), Positives = 629/639 (98%), Strand = Plus / Plus

Query 2 GCGCGCCGGAACGAAGCCGCGGCCCGGCACAGC-ATGGCCCG-CGG-CGGGAGGGCGCT 58  
GCGCGCCGGAACGAAGCCGCGGCCCGGCACAGC ATGGCCCG CGG CGGG GGGCGCT  
Sbjct: 2 GCGCGCCGGAACGAAGCCGCGGCCCGGCACAGCCATGGCCCGCGGGCGGG-GGGCGCT 60

Query: 59 CGGATGTTGGCAGCCTCTGCACTTGGCCCTGCTGCTGCCGGGTGCTCCCGCTCAGC 118  
CGGATGTTGGCAGCCTCTGCTGCTTGGCCCTGCTGCTGCCGGGTGCTCCCGCTCAGC  
Sbjct: 61 CGGATGTTGGCAGCCTCTGCTGCTTGGCCCTGCTGCTGCCGGGTGCTCCCGCTCAGC 120

Query: 119 TGGGATCTCCCGGAGCCCCGACGCCAGCCAGATCCGAGTGCACTCGCGAGGCAAG 178  
TGGGATCTCCCGGAGCCCCGACGCCAGCCAGATCCGAGTGCACTCGCGAGGCAAG  
Sbjct: 121 TGGGATCTCCCGGAGCCCCGACGCCAGCCAGATCCGAGTGCACTCGCGAGGCAAG 180

Query: 179 CTCTGGGCCATGGTCACTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCCCA 238  
CTCTGGGCCA CGTCACTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCCC A  
Sbjct: 181 CTCTGGGCCACGGTCACTTCATGGGCAAGAAGAGTCTGGAGCCTTCCAGCCCATCCCC-A 239

Query: 239 TTGGGGACAGCTCCCCACACCTCCC-TGAGGGACAGGAGCTGAGCTGAGTCATGATCT 297  
TTGGGGACAGCTCCCCACACCTCCC TGAGGGACAGGAGCTGAGCTGAGTCATGATCT  
Sbjct: 240 TTGGGGACAGCTCCCCACACCTCCCC-TGAGGGACAGGAGCTGAGCTGAGTCATGATCT 299

Query: 298 GCTCGGAATCCTCTGCTAAAGAAGGCTCTGGGGGTGAGCCTCAGCCGCCCGCACCCCCA 357  
GCTCGGAATCCTCTGCTAAAGAAGGCTCTGGGGGTGAGCCTCAGCCGCCCGCACCCCCA  
Sbjct: 300 GCTCGGAATCCTCTGCTAAAGAAGGCTCTGGGGGTGAGCCTCAGCCGCCCGCACCCCCA 359

Query: 358 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT-GGGGCA 416  
AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT GGGGCA  
Sbjct: 360 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATAGGGGCA 419

Query: 417 GACACAACAGGTGGCTTAGATTGTGCCCCACCCAGGGAAGGTGCTGAATGGGACCTGTGT 476  
GACACAACAGGTGGCTTAGATTGTGCCCCACCCAGGGAAGGTGCTGAATGGGACCTGTGT  
Sbjct: 420 GACACAACAGGTGGCTTAGATTGTGCCCCACCCAGGGAAGGTGCTGAATGGGACCTGTGT 479

Query: 477 GATGGCCCCATCTGGATGTAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 536  
GATGGCCCCATCTGGATGTAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT  
Sbjct: 480 GATGGCCCCATCTGGATGTAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 539

Query: 537 TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACAGATTATGTTCTGCTGTATTT 596  
TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACAGATTATGTTCTGCTGTATTT  
Sbjct: 540 TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACAGATTATGTTCTGCTGTATTT 599

Query: 597 CCTGCTTCCTGTGTAATTGGTGAATAAAACCTTGCTCTAT 637 (SEQ ID NO: 21)  
CCTGCTTCCTGTGTAATTGGTGAATAAAACCTTGCTCT T (SEQ ID NO: 22)  
Sbjct: 600 CCTGCTTCCTGTGTAATTGGTGAATAAAACCTTGCTCTTT 640 (SEQ ID NO: 23)

**Fig. 4A**

09730617.070301



**BlastX for NOVNEUR:**

ptr:SWISSPROT-ACC:P08949 NEUROMEDIN B-32 PRECURSOR (CONTAINS: NEUROMEDIN B) - Homo sapiens (Human), 121 aa.

Top Previous Match Next Match  
Length = 121

Plus Strand HSPs:

Score = 513 (180.6 bits), Expect = 1.9e-48, P = 1.9e-48  
Identities = 105/118 (88%), Positives = 105/118 (88%), Frame = +2

Query: 44 RREGARMFGSLHLFALLAAGVPLSWDLPEPRSRASKIRVHSRGKLMWIGHFMGKKSLEP 223  
R GARMFGSLH FALLAAGV PLSWDLPEPRSRASKIRVHSRG LMA GHFMGKKSLEP  
Sbjct: 4 RAGGARMFGSLHLFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKSLEP 63

Query: 224 SSPSPILGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQK 397 (SEQ ID NO: 24)  
SSPS G P LRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQK (SEQ ID NO: 25)  
Sbjct: 64 SSPSHWGQLPTPPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQK 121 (SEQ ID NO: 26)

**Fig. 4B**

**ClustalW for NOVNEUR:**

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g., L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

**Sequences used:**

- 1) A37178 (neuromedin B precursor - rat): Locus A37178, accession A37178, PID - g1 12182
- 2) NEUB\_HUMAN (NEUROMEDIN B-32 PRECURSOR): Locus - NEUB\_HUMAN, accession - P08949, PID - g1346684

Neuromedin\_New\_REVCOMP -----VEGSLHFFALLAAGVPLSWDLPEPRSRASKIRVHSRGKLMWIGHFMGKKS  
A37178 MREQGSTWLLRGLLFALFVSCITPEFSDWLPPEPRSRASKIRVHSRGNLWATGHFMGKKS  
NEUB\_HUMAN MARRAGGARVFGSLHFFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS

Neuromedin\_New\_REVCOMP LEPSSPSPLGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQ  
A37178 LEPSSPSPLGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQ---  
NEUB\_HUMAN LEPSSPSHWGLPTPPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQ

Neuromedin\_New\_REVCOMP K (SEQ ID NO: 27)  
A37178 - (SEQ ID NO: 28)  
NEUB\_HUMAN K (SEQ ID NO: 29)

**Fig. 5**

09730517-070001



NOVGON cDNA sequence:

1  
ATGAAGCTGGCATTCCTCTCTCCCTGGCCCCATGGCCCTCCTCCTTCTGGCTGGCTATGGCTGTGTCTCTGGTGCCTCCAG  
81  
TGGGAACCTGGCACTTTGTGGGCTGTGCCGTGAGGGAGTTTACTTTCTGGCCAAGAAGCAGGCTGCAGGGGCTTC  
161  
GGATCACCACGATGCTGTGGGCTGCTGTGAGACTGGGAGAAACCAATTCGGAACCCCCCTATATTGAAGCCCAT  
241  
CATCGAGTCTGTACTACAAAGAGACCAACAGGTGACTGTCAAGCTGCCCAACTGTGCCCGGGAGTGGACCCCTTCTA  
321  
CACCTATCCGCTGGCCATCCGCTGTGACTGGGAGCCCTGCTCCACTGCCACCAAGGAGTGGAGTTGATGCCAGGGGAAG  
401  
CTGCTGTGGCACTGGGCTTCGTGTGTCAAGGTAGGAGACAGGATCTAGGACCAAGGGACCAGGTGGGACATGCACT  
481  
GTAAAGAGACAAGGTGAGTCTCTGAAGGCAGTAGATGTTGGAATGGGCTGCTTGGGGACCCAGCGAGCTCCAGGGGCT  
561  
TTCCTGCTTCTCTGTACCCCTGTATTTCCCTTGGCTTTCCAAATGACTCAGCTTCTGGTAAAGTTGGAACCTTTTCCA  
641  
GCAAAACAGACCTTCATCTTCTCCAGTGCAGAGATTACATTAGGAGGAACATGA (SEQ ID NO: 5)

Fig. 6A

NOVGON Protein Sequence:

MKLAFLFLGPMALLLLAGYGCVLGASSGNLRTFVGCAREFTFLAKKPGCRGLRITTD  
CWGRCEIWEKPILEPPYIEAHRVCTYNETKQVTVKLPNCAPGVDPFYTPVAIRCDG  
ACSTATTLELRMPGEAAVALGFWQRRRQSSRTTGTWRHAAVRDKVSLKAVDGH  
NGLLEDPASQGLSASSCTPVFPLAFQIDSASGKVGNFSSKQTFIFSSAEITLGGT\* (SEQ ID NO: 6)

Fig. 6B

09730617-070901



BlastN for NOVGN:

AF146151 Salmo salar gonadotropin II beta subunit mRNA,  
partial cds - Salmo salar, 266 bp (RNA).

Top Previous Match Next Match  
Length = 266

Plus Strand\_HSPs:

Score = 208 (31.2 bits), Expect = 0.043, P = 0.042  
Identities = 124/205 (60%), Positives = 124/205 (60%), Strand = Plus / Plus

Query: 177 CTGCTGGGGTCCCTGTGAGACCTGGGAGAAACCCATTCGGAACCCCTATATTGAAGC 236  
CTGC G GG C CTG G ACC GGAG CC TT T AA CCC AT TT A C  
Sbjct: 34 CTGCAGTGGCCACTGCGTCACCAAGGAG---CCGGTTTTC-AAGAGCCC-ATTTTCCACC 88

Query: 237 CCAT-C-ATCGAGTCTGTACCTACAACGA-GACCAAAACAGGTGACTGTCAAGCTGCCAA 293  
T C A C GT TG ACCTAC GA G CC A G AC TC CT CC A  
Sbjct: 89 GTGTACCAGCATGTGTGCACTACCGGAGCTCCGCT-ATGAAACGATCCGCTACTCTGA 147

Query: 294 CTGTGCCCCGGAGTCGACCC-CTTCTACACCTATCCCGTGGCCATCCGCTGTGACTGCG 352  
CTGT CCCC G GT GACC C T T CACCTA CC GTGC T GCTGTGACTGC  
Sbjct: 148 CTGTCCCCCTTGGGTGGACCATCATGT-CACCTACCCGTGGCTCTGAGCTGTGACTGCA 206

Query: 353 GAGCCTGTCTCCACTGCCACCAACGAGCTG 381 (SEQ ID NO: 30)  
G CTG CA G CAC C GA CTG (SEQ ID NO: 31)  
Sbjct: 207 GCCTCTGTAACTGGACACTTCTGA-CTG 234 (SEQ ID NO: 32)

Fig. 7A

00736617.070901



BlastX for NOVGON:

P01235 GONADOTROPIN BETA CHAIN PRECURSOR - Cyprinus carpio (Common carp), 144 aa.

Score = 203 (71.5 bits), Expect = 2.3e-16, P = 2.3e-16  
 Identities = 37/85 (43%), Positives = 52/85 (61%)  
 Query: 42 TFLAKKPGC-RGLRITTDACWGRCEWKEPILEPPYIEAHRVCTYNETKQVTVKLNC 100  
           T +K GC + L + T C G C T E P+ + P+ + VCTY + + TV+LP+C  
 Sbjct: 39 TVAVEKEGCPKCLVLQTTICSGHCLTKE-PVYKSPFSTVQHVCTYRDVRYETVRLPDCP 97  
 Query: 101 PGVDPFFYTPVAIRCDOGACSTATTE 126 (SEQ ID NO: 33)  
           PGVDP TYPVA+ CDC C+ T++ (SEQ ID NO: 34)  
 Sbjct: 98 PGVDPHITYPVALS CDCSLCMTDTS 123 (SEQ ID NO: 35)

>ptnr:SWISSNEW-ACC:Q9YGH2 GONADOTROPIN BETA-II CHAIN PRECURSOR (GTH-II-BETA)

- Clupea pallasii (Pacific herring), 149 aa.

Plus Strand HSPs:

Score = 206 (72.5 bits), Expect = 1.0e-15, P = 1.0e-15  
 Identities = 47/117 (40%), Positives = 63/117 (53%), Frame = +1  
 Query: 28 PMALLLLAGYGCVLG--ASSGNLRTFVGCAREFTFLAKKPGC-RGLRITTDACWGRCE 198  
           P +LL CVL A NL+ C+ T +K GC R L T C G C T  
 Sbjct: 5 PECTILLLLCMCVLAVPAQCFNLQP---CVLWNETVSVEKEGCPRLVFRITICSGHCPT 61

Query: 199 WEKPILEPPYIEAHRVCTYNETKQVTVKLNCAPGVDPFFYTPVAIRCDOGACSTATTE 378 (SEQ ID NO: 36)  
           E P+ + P+ + VCTY + T+LP+CA GVDP TYPVA+ C+C CS T++ (SEQ ID NO: 37)  
 Sbjct: 62 KE-PVYKSPFVNVQHVCTYGNFRYETIRLPDCADGVDPVLTYPVALSCSECSLCMDTSD 120 (SEQ ID NO: 38)

>patp:R15106 hCG/bLH chimera, D10 - Homo sapiens, 145 aa.

Plus Strand HSPs:

Score = 188 (66.2 bits), Expect = 5.0e-14, P = 5.0e-14  
 Identities = 40/101 (39%), Positives = 58/101 (57%), Frame = +1  
 Query: 76 SSGNLRTFVGCAREFTFLAKKPGCRG-LRITTDACWGRCEWKE--PILEPPYIEAHR 246  
           S G LR C T A+K C + TT C G C + ++ P++ PP + R  
 Sbjct: 1 SRGPLRPL--CQPINATLAAEKEACPVCITFTTISICAGYCPMKRVLPLVILPMPQ---R 55

Query: 247 VCTYNETKQVTVKLNCAPGVDPFFYTPVAIRCDOGACSTATTE 378 (SEQ ID NO: 39)  
           VCTY+E + +V+LP C PGVDP ++PVA+ C CG C ++T+ (SEQ ID NO: 40)  
 Sbjct: 56 VCTYHELRFASVRLPGCPPGVDPMVSFPVALSCHCGPRLSSTD 99 (SEQ ID NO: 41)

>patp:W65110 Equine chorionic gonadotropin beta-chain protein - Equus caballus, 169 aa.

Plus Strand HSPs:

Score = 175 (61.6 bits), Expect = 1.2e-12, P = 1.2e-12  
 Identities = 43/116 (37%), Positives = 60/116 (51%), Frame = +1  
 Query: 31 MALLLLAGYGCVLGASSGNLRTFVGCAREFTFLAKKPGCR-LRITTDACWGRCEWKE 207  
           + L +L G V AS G LR C T A+K C + TT C G C + +  
 Sbjct: 7 LLLWMLLSVGGVW-ASRGPLRPL--CRPINATLAAEKEACPICITFTTISICAGYCPMVR 63

Query: 208 PILEPPYIEAHR-VCTYNETKQVTVKLNCAPGVDPFFYTPVAIRCDOGACSTATTE 378 (SEQ ID NO: 42)  
           + P + A + VCTY E + +++LP C PGVDP ++PVA+ C CG C TT+ (SEQ ID NO: 43)  
 Sbjct: 64 VM--PAALPAIPQPVCTYRELRFASIRLPGCPPGVDPMVSFPVALSCHCGPQCIKTD 119 (SEQ ID NO: 44)

Fig. 7B

09730617.076904

# ClustalW alignment for NOVGNON:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

GTHB CYPCA	MGTPVVRHLMVRNHIIFSVMVLAFAVSS---	YLEPCEPVNNEIVAEKEGCPKCLVLOTHI
Q98849 GTHB2_GOLDFISH	MGTPVVRHLMV---IFSVMVLAFAVSS---	YLEPCEPVNNEIVAEKEGCPKCLVLOTHI
LSHB BOVIN	MEIPCCSLHW---LLLEVGWASRGV---	LRELCCPINATIAAEKBACFVCITFTTISI
LSHB SHEEP	MEMLQCSLHW---LLLGWAGWASRGV---	LRELCCPINATIAAEKBACFVCITFTTISI
novel_gonadotropin	MMHAPLFLGPMALLLIAGYGVLEASSGNLRTFVGAVREFTFLAKKPGCRG-LRIITDA	
GTHB CYPCA	CSGHCLT-KBPVYKSPSESTNYCHVCTYRDVRYETVRLPCPPGVDPHITYPVALSCDCSL	
Q98849 GTHB2_GOLDFISH	CSGHCLT-KBPVYKSPSESTNYCHVCTYRDVRYETVRLPCPPGVDPHITYPVALSCDCSL	
LSHB BOVIN	CAGYVCPG-MKRVLPVILPPVQPVCTYHETFAFVRLPCPPGVDPVMSFPVALSCHCCP	
LSHB SHEEP	CAGYVCLS-MKRVLPVILPPVQPVCTYHETFAFVRLPCPPGVDPVMSFPVALSCHCCP	
novel_gonadotropin	QWGRG-TWEKPTLEPPMIEBAHRVCTYNETKQVIVRLPCAGVDPVPTYPVAIRCDCCGA	
GTHB CYPCA	GRMDTS-----CT-----IESLPDFQMSQ-REDPLVY-----	
Q98849 GTHB2_GOLDFISH	GRMDTS-----CT-----IESLPDFQMSQ-REDPLVY-----	
LSHB BOVIN	CRHSST-----CG-----ERTQLACDHPPLDILFI-----	
LSHB SHEEP	CRHSST-----CG-----ERTQLACDHPPLDILFI-----	
novel_gonadotropin	ESTATTELRLMPGEAAVALGFWCQRRROSRITGTWRWHAADVQKVSLLKAVDGNWGLLG	
GTHB CYPCA	-----	(SEQ ID NO: 45)
Q98849 GTHB2_GOLDFISH	-----	(SEQ ID NO: 46)
LSHB BOVIN	-----	(SEQ ID NO: 47)
LSHB SHEEP	-----	(SEQ ID NO: 48)
novel_gonadotropin	DPASSQGLSASSCTPVFPLAFQIDSASGKGVNFSSQTFIFSSABITLGGT	(SEQ ID NO: 49)

Fig. 8

## NOVINTRA A cDNA sequence:

Regions 116708 to 116812 (1-105bp), 117121 to 117248 (106-233p), and 117529 to 117778 (234-483bp).

CACCTGTCTACTGTGTTTCAGAAATTAATATGCAGACCAAGGCTCTATACACAAGAG  
ATGGCCAGCTGCTGGTGGGAGATCTCTGTTGCAGACCACTGCTGTGCAGAGAAGATC  
TGCACTACTTCTAAACAGAGGCTTGGCCCGCACCAAGGTCCCATTTTCTGGGGATC  
CAGGGAGGGAGCCGCTGCTGGCATGTGTGGAGACAGAGAGGGGCTTCCCTACAG  
GCTGGAGCCATCCACCTTGCCCCCAAGAGATGTGAACATTGAGGAACGTGACAAAG  
GTGGTGAAGAGGCCACACGCTTCACTTCTTCCAGAGCAGCTCAGGCTCCGCTTCA  
GGCTTGAGGCTGCTGCTGGCTGGCTGGCTTCTGTGTGGCCCGGAGAGCCCCAGC  
AGCCAGTACAGCTACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTTTACTTTG  
AACAGAGCTGTAAGGAGACAGGAACTGC (SEQ ID NO: 7)

Fig. 9A

## NOVINTRA A Protein sequence:

LSYCFRIKYADOKALYTRDQQLVGDPPVADNCCAEXICILPNRGLARTKVPFLIGIOGGS  
RCLACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEEATRTFFQSSSGSAFRLEAAAWP  
GWFLCGPAEPQQPVLTKSEPSARTKIFYEQSW (SEQ ID NO: 8)

Fig. 9B



BlastN for NOVINTRA A:

gb:GENBANK-ID:AF072476|acc:AF072476 Equus caballus interleukin-1 receptor  
antagonist secretory form (IL-1ra) gene, partial cds - Equus caballus,  
221  
bp.

Top Previous Match Next Match

Length = 221

Plus Strand HSPs:

Score = 321 (48.2 bits), Expect = 8.1e-08, P = 8.1e-08

Identities = 147/218 (67%), Positives = 147/218 (67%), Strand = Plus / Plus

Query: 253 AGGATGTGAACATTGAGGAAGTACAA-AGTGGTGAAGAGGCCACAGCTTCACTTC 311  
AGG GT AACAT GA CTG CAA A G GA GAG CA CGCTTCACTTC  
Sbjct: 4 AGGCAGTTAACATCACTGACCTGAGCAAGAACAAG-GAGGAGACAAGCGCTTCACTTC 62

Query: 312 TTCCAGAGCAG-CTCAGGCTCCGCTTCAGGCTT-GAGGCTGCTGCCTGGCTGGCTGGT 369  
TCC G CA C GGC CC CC CAG CTT GAG CTGC GCCTG CTTGGCTGGT  
Sbjct: 63 ATCC-GCTCAAAACAGTGGCCCCACCACAG-CTTCGAGTCTGCCGCTGGCTGGCTGGT 120

Query: 370 TCCTGTGTGGCCCGGCAG-AGCCCCAGCAGCCAGTACAGC-TCACCAAGGAG---AGTGA 424  
TCCT TG CG CAG AG C A C GCC GT CAGC TCACCAA AG A GA  
Sbjct: 121 TCCTCTGTCAAGGCG-CAGGAGGCAGACGGCCCGT-CAGCCTCACCACAAGCCCAAGA 178

Query: 425 GCCCT-CAGCCCGT-ACCAAGTTTACTTTGAACAGAGCTGGTAG 467 (SEQ ID NO: 50)  
G CCT CA GT ACCAAGTT TACTT A AG C GTAG (SEQ ID NO: 51)  
Sbjct: 179 GTCCCTTCATG--GTACCAAGTTCTACTTCCAGGAGGACAGTAG 221 (SEQ ID NO: 52)

Fig. 10A

00730617-070901



**BlastX for NOVINTRA A:**

ptnr:TREMBLNEW-ACC:CAB59831 IL-1L1 PROTEIN - Mus musculus (Mouse), 155 aa.

Top Previous Match Next Match

Length = 155

Plus Strand HSPs:

Score = 309 (108.8 bits), Expect = 8.0e-27, P = 8.0e-27

Identities = 70/149 (46%), Positives = 93/149 (62%), Frame = +3

Query: 12 CFIKYADQKALYTRDQQLLVGDPVADNCC-AEKICILPNRGLARTKVPILFGIQGSSRC 188

CFR+K + K LY + QLL G A+ E+I ++PNR L + P+ LG+QGS+C

Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHAEKVIKGEETSVVPRALDASLSPVILGVQGSQC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEATRTFFQSSSGSAFRLEAAAWPGW 368

L+C TE+GP L+LEP VNI ELY G +E+ PTF++ G E+AA+PGW

Sbjct: 68 LSC-GTEKSPILKLEP-----VNIMELYLGAKESKSPTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQPPVQLTKESEPSAR---TKFYFEQ 458 (SEQ ID NO: 53)

FLC E QPV+LT+ E A T FYF+Q (SEQ ID NO: 54)

Sbjct: 120 FLCTSPADQPVRLTQIPEDPAWDAPITDFYFQQ 153 (SEQ ID NO: 55)

>ptnr:SPREMBL-ACC:Q9UBH0 FIL1 DELTA (INTERLEUKIN-1 LIKE PROTEIN 1)  
(INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG 1) (INTERLEUKIN-1 DELTA) - Homo  
sapiens (Human), 155 aa.

Plus Strand HSPs:

Score = 285 (100.3 bits), Expect = 4.3e-24, P = 4.3e-24

Identities = 67/149 (44%), Positives = 89/149 (59%), Frame = +3

Query: 12 CFIKYADQKALYTRDQQLLVGDPVADNCC-AEKICILPNRGLARTKVPILFGIQGSSRC 188

CFR+K + K LY + QLL G A E+I ++PNR L + P+ LG+QGS+C

Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHAGKVIKGEETSVVPRWLDASLSPVILGVQGSQC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEATRTFFQSSSGSAFRLEAAAWPGW 368

L+C +E P+L LEP VNI ELY G +E+ PTF++ G E+AA+PGW

Sbjct: 68 LSCGVQE-PITLLEP-----VNIMELYLGAKESKSPTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQPPVQLTKESEPSAR---TKFYFEQ 458 (SEQ ID NO: 56)

FLC E QPV+LT+ E T FYF+Q (SEQ ID NO: 57)

Sbjct: 120 FLCTVPEADQPVRLTQLPENGWNAPIITDFYFQQ 153 (SEQ ID NO: 58)

Fig. 10B

09730617-070964



ClustalW for NOVINTRA A:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) X86458spoil1 (cDNA encoding a human spoil-I protein); X86459spoil2 (cDNA encoding a human spoil-II protein); X89432-illdelta (human IL-1 delta encoding cDNA); Q14628 (intracellular IL-1 receptor antagonist type II-human); G512010illbeta (ovine IL-1 beta - pig)

```
X86458spoil1      -----DNHTVIRGTPGDA-----DGG--GRAVYGS-----
X86459spoil2      -----DNHTVIRGTPGDA-----DGG--GRAVYGSSESNAVGMGLWLRPSALTLSPV
X89432-illdelta   -----MALADLYEEG-----CGG--GGGEDNADSK-----E-----
Q14628
illbeta-1DNA
G512010illbeta    MATVPEPINSWYAYSDENELLFEVDCPKQMSCTCHLDLGSMGDGNIQLQISHQLYNKS

X86458spoil1      -----MCPITGITINDLNCVHTLOGQNLVAVPRSDS--VTPVIVAVIT
X86459spoil2      EAPAFSAPLCTLPFPFVCPITGITINDLNCVHTLOGQNLVAVPRSDS--VTPVIVAVIT
X89432-illdelta   -----MVLSCALCFPMKSGALVMTVHNNQLTAGGLHA---GKVIKGEPI
Q14628            -----TICRPSGRKSSVQAFRIIDNMTFYIUNNQLVAGYLG---PNINLEBK
illbeta-1DNA      -----GPSALSYCFRIKYADQALVTRDGLLVDPVA---DNCCREKI
G512010illbeta    FRQVSVIVAMEKLRSRAYEHVFRDDDRSILSFIFEEEPVIFETSDELLCDAAVQSVK

X86458spoil1      CKYFAL-----EGRGDETYLGTGNPDM
X86459spoil2      CKYFAL-----EGRGDETYLGTGNPDM
X89432-illdelta   SVMNPN-----LDASLSEMLGVCCGSO
Q14628            DVMF-----IEPHALFLGLHGGK
illbeta-1DNA      CIEPNRG-----LARTKVPITFLGIQCCSR
G512010illbeta    CKQPRBOKSLVLDSPCVLKALHLLSQEMSRREVFCMSFVQGEERDNKIEVALGIRDKNL

X86458spoil1      CLYQKVGCEPTLOLE-----QNTMDLYGQPEVPKPELFYRAKTCRISTLESVAEPD
X86459spoil2      CLYQKVGCEPTLOLE-----QNTMDLYGQPEVPKPELFYRAKTCRISTLESVAEPD
X89432-illdelta   CLSCG-VCGEPITLLEP-----VNIMELYLGAKESSFTFYRDMGLTSFESAAHFG
Q14628            CLSCVKSCGEPITLOLE-----VNIIDLSENRKQDGRPAITRSDGCPITSFESAAHFG
illbeta-1DNA      CLACVETEECPISLOLEPSTLPQCVNIELYKGGDEATRFPTFGSSGSAFRLCAAMFG
G512010illbeta    YLSCVHKEPTLOLE-----VDPKVPKRNMRGRVETKTEIKNVFESVLYN

X86458spoil1      WFFHSS-KRQDEHILTSBLCKS-----YNTAEELNIN- (SEQ ID NO: 59)
X86459spoil2      WFFHSS-KRQDEHILTSBLCKS-----YNTAEELNIN- (SEQ ID NO: 60)
X89432-illdelta   WFLCTVPEADDEPRLTOLPENGWNPATIDVEYQCC- (SEQ ID NO: 61)
Q14628            WFLCTIAMEADQVSTINMPDEG---VMVTKFYBDE- (SEQ ID NO: 62)
illbeta-1DNA      WFLGPAEPQDPVLTKESEPS---ARKIKYBQSW- (SEQ ID NO: 63)
G512010illbeta    WFLTSQIBKPVRLGRFRGQ---DIDERMETLSF (SEQ ID NO: 64)
```

Fig. 11

09730617-070901



**NOVINTRA B cDNA sequence:**

Regions 116968 to 117028 (1-61bp), 104067 to 104164 (62-159bp), 101958 to 102098 (160-300bp), and 100915 to 101134 (301-520bp) of genomic clone (-frame).

ATGGGCACACCTGGCCTGGCCCTGCATGCAGACTGGACGGTGAGCCAGGACTTCTG  
CAGGACACCCAAATCCTATGCTATTTCGTGATTCTCGACAGATGGTGTGGGTCCTGAG  
TGGAATTCCTTAATAGCAGCTCCTCTTAGCCGCAGCATTAAAGCCTGTCACTCTTCAT  
TTAATAGCCTGTAGAGACACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTA  
CCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC  
TACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC  
AGAAGCCCTTTCTCTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTTTCAGTCAGT  
CTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAGGACAGCCCATCTTTCTC  
ACCAAGGAGAGAGGCATAACTAATAACACTAACTTCTACTTAGATTCTGTGGAATA  
AATCCAGC (SEQ ID NO: 9)

**Fig. 12A**

**NOVINTRA B Protein sequence:**

MGTPGLALHADWTVSQDFCRTPKSYAIRDSRQMWWVLSGNSLIAAPLSRSIKPVTLHLI  
ACRDTEFSDKEKGNMVLGKIGKDLCLFCAEIQ GKPTLQLKEKNIMDLYVEKKAQKPFL  
FFHNKEGSTSVFQSVSPGWFIATSTTSGQPIFLTKERGITNNTNFYLDSE (SEQ ID NO: 10)

**Fig. 12B**

09730617.070901



**BlastN for NOVINTRA B:**

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,  
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Plus Strand\_HSPs:

Score = 309 (46.4 bits), Expect = 1.1e-07, P = 1.1e-07

Identities = 197/331 (59%), Positives = 197/331 (59%), Strand = Plus / Plus

Query: 169 CATTTAATAGCCTGTA-GAGAC-ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTT 226  
CA TA TA CTG A GAGA A AGA T GTG C G AG T AT T GT T  
Sbjct: 217 CAAATACTAACTGGAAGAGAAGATAGATGTG-GTGCCCT--GTGAGCCTCATTTTGTGT 273

Query: 227 ACCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC-T 285  
CCTGGG ATC A GGA A CT TG CT T CTGTG AA T C GG A G T  
Sbjct: 274 TCCTGGGGATCCATGGAGGGAAGCTGTGCCTGTCTGTGTC-AAGT-CTGGTGATGAGAT 331

Query: 286 -ACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC-AGA 343  
A T CAG T A G A AA ATCA GACCTG A GA AG AGCA A A  
Sbjct: 332 GAAGCTCCAGTTGGACGCAGTTAACATCACAGACCTG-AGAAAGAACAGCGAGCAGGACA 390

Query: 344 AGCCCTTTCTCTTTTCCACAATAA-AGAAGGCTCCACTTCTGTCTTTTCAGTCAGTCTCT 402  
AGC CTT CTT TCC C A AG GGC CCAC C CTTT AGTCAG C C  
Sbjct: 391 AGCGCTTCACCTTCATCCGCTCCGACAGT-GGCCCCACCACCAGCTTTGAGTCAGCCGCC 449

Query: 403 TACCCTGGCTGGTTTCATAGCCACCTCCACCACAT-CAGGACAGCCCATCTTTCTCACCAA 461  
T CTTGGCTGGTTC T CAC T CAC A A CAG CAGCC T CTCACCAA  
Sbjct: 450 TGTCTCTGGCTGGTTCTCTGCAC-TGCACTAGAGGCAGACCAGCCTGTTGGCCTCACCAA 508

Query: 462 GGAGAG-AG-GCATAACT-AATAACACTAACTTCTACTT 497 (SEQ ID NO: 65)  
G A GCA T AA CAC AA TTCTACTT (SEQ ID NO: 66)  
Sbjct: 509 CACGCCCAAAGCAGCCGTCAAGGTCACCAAGTTCTACTT 547 (SEQ ID NO: 67)

**Fig. 13A**

09730617-070901



**BlastX for NOVINTRA B:**

>ptnr:SPTREMBL-ACC:Q9UHA5 FIL1 ETA - Homo sapiens (Human), 157 aa.  
Plus Strand HSPs:

Score = 777 (273.5 bits), Expect = 3.2e-76, P = 3.2e-76  
Identities = 149/149 (100%), Positives = 149/149 (100%), Frame = +1

Query: 64 PKSYAIRDSRQMVVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTFSDKEKGNMVYLGIGK 243  
PKSYAIRDSRQMVVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTFSDKEKGNMVYLGIGK  
Sbjct: 9 PKSYAIRDSRQMVVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQQKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 423  
KDLCLFCAEIQQKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA  
Sbjct: 69 KDLCLFCAEIQQKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 128

Query: 424 TSTTSGQPIFLTKEGKITNNTNFYLDVSE 510 (SEQ ID NO: 68)  
TSTTSGQPIFLTKEGKITNNTNFYLDVSE (SEQ ID NO: 69)  
Sbjct: 129 TSTTSGQPIFLTKEGKITNNTNFYLDVSE 157 (SEQ ID NO: 70)

>ptnr:SPTREMBL-ACC:Q9NZH7 INTERLEUKIN-1 HOMOLOG 2 - Homo sapiens (Human), 164 aa.  
Plus Strand HSPs:

Score = 411 (144.7 bits), Expect = 1.9e-37, P = 1.9e-37  
Identities = 80/85 (94%), Positives = 81/85 (95%), Frame = +1

Query: 64 PKSYAIRDSRQMVVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTFSDKEKGNMVYLGIGK 243  
PKSYAIRDSRQMVVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTFSDKEKGNMVYLGIGK  
Sbjct: 9 PKSYAIRDSRQMVVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQQKPTLQLKEKNIMD 318 (SEQ ID NO: 71)  
KDLCLFCAEIQQKPTLQLK + D (SEQ ID NO: 72)  
Sbjct: 69 KDLCLFCAEIQQKPTLQLKLQGSQD 93 (SEQ ID NO: 73)

>ptnr:TREMBLNEW-ACC:AAF02757 INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG  
- Homo sapiens (Human), 155 aa.

Top Previous Match Next Match  
Plus Strand HSPs:

Score = 197 (69.3 bits), Expect = 5.9e-15, P = 5.9e-15  
Identities = 52/147 (35%), Positives = 76/147 (51%), Frame = +1

Query: 73 YAIRDSRQMVVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTFSDKEKGNMVYLGIGK 252  
+ ++DS V L N L+A L K+ I+ + D ++ LG++G  
Sbjct: 9 FRMKDSALKVLYLHNNQLLAGGLHAG-KVIKGEIISVPPNRWLDASLSPVI-LGVQGSQ 66

Query: 253 CLFCAEIQQKPTLQLKEKNIMDLVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIATST 432  
CL C Q +PTL L+ NIM+LY+ K K F F+ G TS F+S +YPGWF+ T  
Sbjct: 67 CLSCGVGQ-EPTLTLEPNIMELYLGAKESKSTFYRRDMGLTSSFESAAYPGWFLCTVP 125

Query: 433 TSGQPIFLT- -ERGITNN- -TNFYLDVSE 510 (SEQ ID NO: 74)  
+ QP+ LT+ E G N T+FY + (SEQ ID NO: 75)  
Sbjct: 126 EADQPVRLTQLPENGWGNAPITDFYFQQCD 155 (SEQ ID NO: 76)

Fig. 13B

09730617-070601





# ClustalW for NOVINTRA B:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

## Sequences used:

- 2) X86459spoil2 (cDNA encoding a human spoil-II protein; Q14628 (intracellular IL-1 receptor antagonist type II-human); AAF02757 (intracellular IL-1 receptor antagonist type II-human); G512010; (OVINE IL-1 BETA - Pig)

## Multiple Alignment:

```

illbeta2DNA      -----MCPELALHADWTVSQD-----
X86459spoil2     -----DNHTMRGPPDADGGGRAVTSSESN-----
Q14628           -----MALADLYEEGGGGGEGEDNADSKE-----
AAF02757
G512010illbeta   MATVPPEPINEVMAYYSDENELLFEVDGPKQMKSTQHLDLGMDGNIQLQISHLYNKS

illbeta2DNA      -----FQRT-----EKSYAIR-----
X86459spoil2     AVGMGLWRLRPSALTLSPVEAPAFSAPLSTLPFPVPCK-EITGTIN-----
Q14628           -----TICRPSGRKSSK-MQAFRIW-----
AAF02757         -----MVLSG-ALCFRMK-----
G512010illbeta   FRQVVSIVIVAMEKLRSRAYEHVFRDDDLRSILSFIFEEDVIFETSSDELLCDAVQSVK

illbeta2DNA      ----DSROMVAVLSGNSLIAPPSRSIKPVHLHACRDTEFSDK-EKGNMVELGIGKD
X86459spoil2     ----DLNQVATLQGNLVAVPRSDSVTFVAVATCKYPEALEQ-GRGDEYVLGIQNP
Q14628           ----LVNOKTEYLRNNELVAGYIQ--GPNVNLEEKIDVVF-----IEPHAEELGIIHGK
AAF02757         ----DSATKLYLHNNELLAGGH--AGKVIKGEESVVENRWLD-ASLSPVILGVQCGS
G512010illbeta   CKLDREQKSLVDS-POVLKATHLLSQEMSREVMQMSFVQGGSERDNKIPVAGIRDKN

illbeta2DNA      ECLFOAEIQGNPTLQLKEKNIMDLYVEKKAORPESEFHNKGGSTSMFCQSVSYPGWFIATS
X86459spoil2     NCLYCBKIVGCEPTLQLEKEKIMDLYGCPEPVKPESEFYRAKTGRTSHLESVAFPDWFIIASS
Q14628           NCLSOVLSSEDETLQLEAVNTIDLSNRKQDKRAFIIRSDSPTTFSPESAAPCGWFQDA
AAF02757         QCCLSCG-VGQEPPTLILEPVNIMELYLGAKESRSFTFYRRDMGLTSSFPESAAYPGWFQCTV
G512010illbeta   EYLSQVVRGSDPTLQLEEDPKVYP-KRNMGRVRFYKTEIKNTVBFESVLYPNWYISTS

illbeta2DNA      TTSGQPHFLTKER--G--ITNNTNFIILDSVE- (SEQ ID NO: 77)
X86459spoil2     KRQ-QPHILISEL--G--KSYNTAFELNIND- (SEQ ID NO: 78)
Q14628           MEADQPVSLTNMPDEG--VMVKKFYQEDE- (SEQ ID NO: 79)
AAF02757         PEADQPVRLTOLPENCGWNAPITDEYFQOCD- (SEQ ID NO: 80)
G512010illbeta   QIEKEPVILGRFR--G--GQIDIDRMETLSP (SEQ ID NO: 81)
```

Fig. 14

09730617.070501



NOVINTRA C cDNA sequence:

Region 168700 to 168880 (1-181bp), 169967 to 170118 (182-331bp) and 170635 to 170694 (332-391bp) of the genomic clone (- frame).

GATATCAATCATCGGGTGTGGGTCTTCAGGACCAGACGCTCATAGCAGTCCCCGAGG  
AAGGTGTTCCCGAGTCACTATTGCCTTAATCTCATGCCGACATGTGGAGACCCCTTGAG  
AAAGACAGAGGGAACCCCATCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGAT  
GTGTGCTAAAGTCGGGGACCAGCCACACTGCAGCTGAAGCTTCAGGAAAAGGATA  
TAATGGATTTGTACAACCAACCCGAGCCTGTGAAGTCCTTTCTCTTACCACAGCC  
AGAGTGGCAGGAACCTCCACCTTCGAGTCTGTGGCTTCCCTGGCTGGTTCATCGCTG  
TCAGCTCTGAAGGAGGCTGTCTCTCATCCTTACCCAAGAACTGGGGAAAG (SEQ ID NO: 11)

Fig. 15A

NOVINTRA C Protein sequence:

DINHRVWVLQDOTLIAVPRKVFPVTIALISCRHVETLEKDRGNPIYLGNLNLCLMCAK  
VGDQPTLQLKLEKDIMDLYNQPEPVKSFLFYHSQSQRNSTFESVAFPGWFIASSEGCG  
PLILTQELGK (SEQ ID NO: 12)

Fig. 15B

BlastN for NOVINTRA C:

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,  
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Minus Strand-HSPs:

Score = 274 (41.1 bits), Expect = 5.6e-06, P = 5.6e-06

Identities = 150/244 (61%), Positives = 150/244 (61%), Strand = Minus / Plus

Query: 258 TCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGATGTGTGCTAAAGTCGGG-GACCAG 200  
T T CCTGGG T ATGGA AA CT TGCCTG TGTG T AAGTC GG GA AG  
Sbjct: 271 TGTTCCTGGGGATCCATGGAGGGAAGCTGTGCCTGTCTCTGTG-TCAAGTCTGGTGATGAG 329

Query: 199 CCCACACTGCAGCTGAAGCTTCAGGAAAAGGATATAATGGATTGTACAACCAACC-CGA 141  
A CT CAG TG A C CAG AA AT A GA TG A AA AAC CGA  
Sbjct: 330 ATGAAGCTCCAGTTGGA-CG-CAGTTAAC----ATCACAGACCTG-AGAAAGAACAGCGA 382

Query: 140 GCCTGTGAAGTCCTTTCTCTTCTACCACAGCCAGAGTGGCAGGAATCCACCTTCGAGTC 81  
GC G AAG CTT CTTC CC C C A AGTGGC A C CCA CTT GAGTC  
Sbjct: 383 GCAGGACAAGCGCTTCACCTTCATCCGCTCCGACAGTGGCCCCACCACAGCTTTGAGTC 442

Query: 80 TGTGGCTTTCCCTGGCTGGTTTCATCGCTGT-CAGCTCTGAAGG-AGGCTGTCTCTCATC 23  
G GC T CTTGGCTGGTTC TC TG C GC CT AGG AG C CCT T C  
Sbjct: 443 AGCCGCTGTCTGTGGCTGGTTCCTC--TGCACTGCACTAGAGGCAGACCAGCCTGTTGGC 500

Query: 22 CTTACCCA 15 (SEQ ID NO: 82)  
CT ACC A (SEQ ID NO: 83)  
Sbjct: 501 CTCACCAA 508 (SEQ ID NO: 84)

Fig. 16A

05730617-070901



**BlastX for NOVINTRA C:**

>ptnr:SPTREMBL-ACC:Q9UHA7 FIL1 EPSILON - Homo sapiens (Human), 158 aa.  
Plus Strand HSPs:

Score = 646 (227.4 bits), Expect = 2.4e-62, P = 2.4e-62  
Identities = 126/130 (96%), Positives = 127/130 (97%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYGLNGLNLCMC 174  
DINHRVWVLQDQTLIAVPRK + PVTIALISCRHVETLEKDRGNPIYGLNGLNLCMC  
Sbjct: 17 DINHRVWVLQDQTLIAVPRKDRMSPVTIALISCRHVETLEKDRGNPIYGLNGLNLCMC 76

Query: 175 AKVGDQPTLQLKLEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 354  
AKVGDQPTLQLK EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG  
Sbjct: 77 AKVGDQPTLQLK--EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 134

Query: 355 GCPLILTQELGK 390 (SEQ ID NO: 85)  
GCPLILTQELGK (SEQ ID NO: 86)  
Sbjct: 135 GCPLILTQELGK 146 (SEQ ID NO: 87)

>ptnr:SPTREMBL-ACC:Q9NZH8 INTERLEUKIN-1 HOMOLOG 1 - Homo sapiens, 169 aa.

Plus Strand HSPs:

Score = 416 (146.4 bits), Expect = 5.7e-38, P = 5.7e-38  
Identities = 82/130 (63%), Positives = 101/130 (77%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYGLNGLNLCMC 174  
D+N +VW LQ Q L+AVPR V PVT+A+I+C++ E LE+ RG+PIYLG+ +CL C  
Sbjct: 29 DLNQVWVLQGGQNLVAVPRSDVTPTVAVITCKYPEALEQGRGDPYLGIQNPENCLYC 88

Query: 175 AKVGDQPTLQLKLEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 354  
KVG+QPTLQLK E+ IMDLY QPEPVK FLFY +++GR ST ESVAFP WFIA SS+  
Sbjct: 89 EKVGEQPTLQLK--EQKIMDLYGQPEPVKPFIFYRAKTGRSTLESVAFPDWFIA-SSKR 145

Query: 355 GCPLILTQELGK 390 (SEQ ID NO: 88)  
P+ILT ELGK (SEQ ID NO: 89)  
Sbjct: 146 DQPIILTSGLK 157 (SEQ ID NO: 90)

>ptnr:SWISSPROT-ACC:P25085 INTERLEUKIN-1 RECEPTOR ANTAGONIST PROTEIN  
PRECURSOR (IL-1RA) (IL-1RN) (IRAP) - Mus musculus (Mouse), 178 aa.

Top Previous Match Next Match

Minus Strand HSPs:

Score = 173 (60.9 bits), Expect = 2.1e-12, P = 2.1e-12  
Identities = 35/81 (43%), Positives = 50/81 (61%), Frame = -1

Query: 259 IYGLNGLNLCMC AKVGDQPTLQLKLEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFES 80  
++LG++G LCL CAK GD ++L+L+E +I DL E K F F S+ G ++FES  
Sbjct: 82 VFLGIHGKLCCLCAKSGDD--IKLQLEEVNITLDSKNKEEDKRFTFIRSEKGPPTS FES 139

Query: 79 VAFPGWFIASSEGCGPLILT 17 (SEQ ID NO: 91)  
A PGWF+ + E P+ LT (SEQ ID NO: 92)  
Sbjct: 140 AACPGWFLCTTLEADRPVSLT 160 (SEQ ID NO: 93)

**Fig. 16B**

05730617-070901



# ClustalW for NOVINTRA C:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

## Sequences used:

- 1) IL1X\_MOUSE: Locus - IL1X\_MOUSE: Accession - P25085; PID - g124313
- 2) IL1X\_HORSE: Locus - IL1X\_HORSE: Accession - 018999; PID - g6166230
- 3) AAF02757\_HUMAN: Locus - AF186094\_1; Accession - AAF02757; PID - g6049805

```
IL1X_MOUSE      MEICWGPYSHLISLILLLFSEAACRPSGKRPCCKMOAFRIWDTNOKIFLYLRNNOLIAGY
IL1X_HORSE      MEIRRRSVRHLISLILLLFLEYSETACHPLGKRPCCKMOAFRIWDMNOKIFYMRNNQLVAGY
AAF02757 Human -----MVLSCATC-----FMKMSALKVILTHNNOLLAGG
Novel_IL1       -----LINHRVWVLQDQTLTAVP-----

IL1X_MOUSE      LOGPNIKLE---EKIDVVF---TDLHSVFLGIHGGKLCCLSCAKSGDEIKLQLEEVN-
IL1X_HORSE      LQESNTKIQ---EKIDVVF---TDPDALFLGLHGRKLCCLSCAKSGDEINFLBAVN-
AAF02757 Human LHAGKVIKG---EELSVVENRWLDASLSPVILGVCGGSCCLSCG-VGQEPTEILEPVN-
Novel_IL1       RKVFPVITHALISCRHVETLEK---DRGNPILGLNGLNCLNCAKVEDQPTLQLKQEK

IL1X_MOUSE      -ITDLSKNKEEDKRFTFIRSENGPTISFESAACPGWFLCTALEADRVPVSLTHPEE---P
IL1X_HORSE      -ITDLSKNKEENKRFTFIRSENGPTISFESAACPGWFLCTALEADRVPVSLTHPRKE---S
AAF02757 Human TMBIYLGAKEKSGSTFYRDMGLISFESAAMPGWFLCTVPEADQPVRLTQLPENGAWN
Novel_IL1       DTMOLIYNQEPVVKSLFVHSQSGRNHIFESVAPGWETAVSSSEGQPAITLTELKGLK---

IL1X_MOUSE      LKVTKFVFOEDC (SEQ ID NO: 94)
IL1X_HORSE      FKVTKFVLOEDC (SEQ ID NO: 95)
AAF02757 Human AKHIDFYFOQCD (SEQ ID NO: 96)
Novel_IL1       ----- (SEQ ID NO: 97)
```

Fig. 17

09730617.070901

09730617 070901

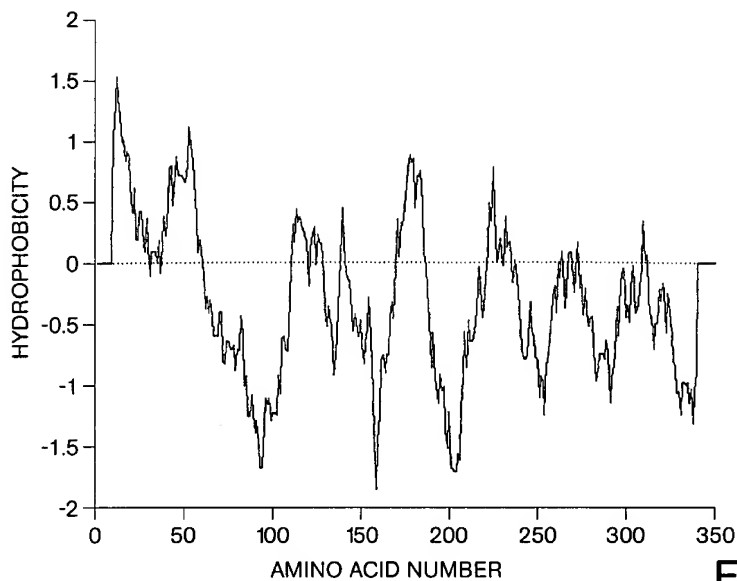


Fig. 18

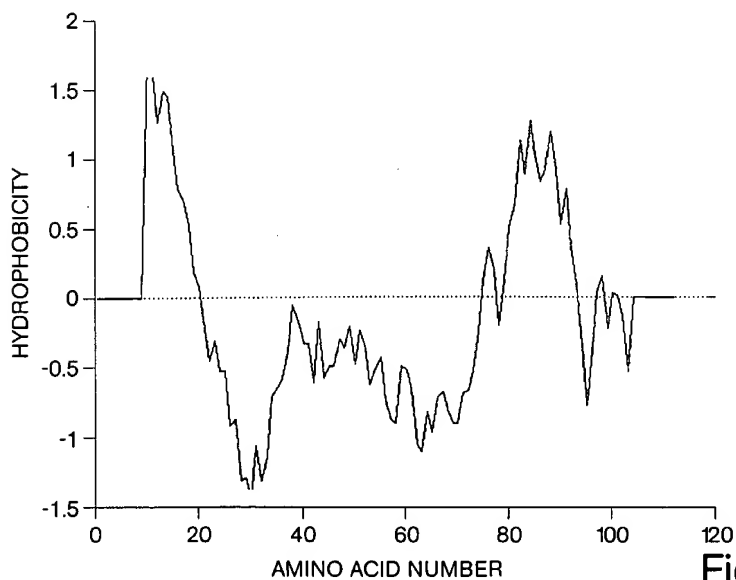


Fig. 19

09730617-070901

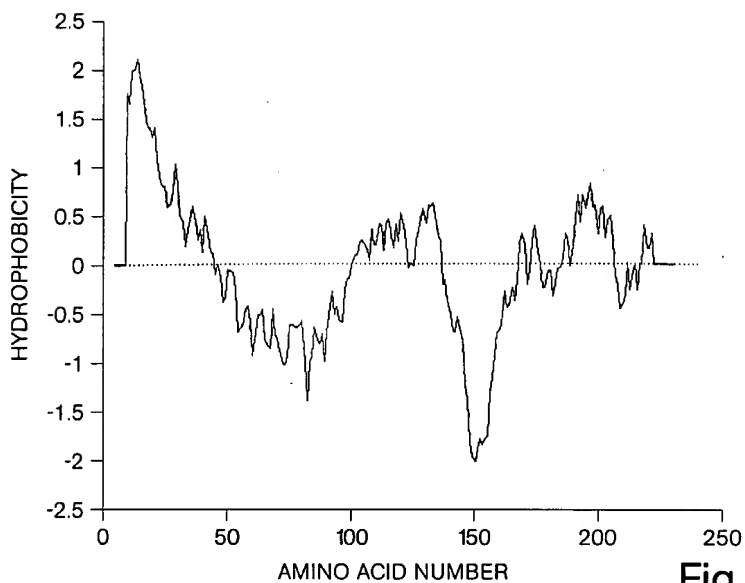


Fig. 20

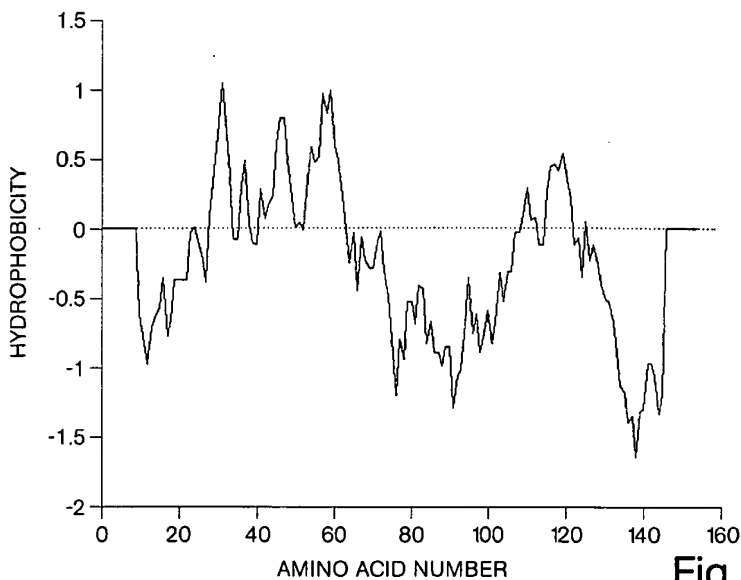


Fig. 21

106020-47905600

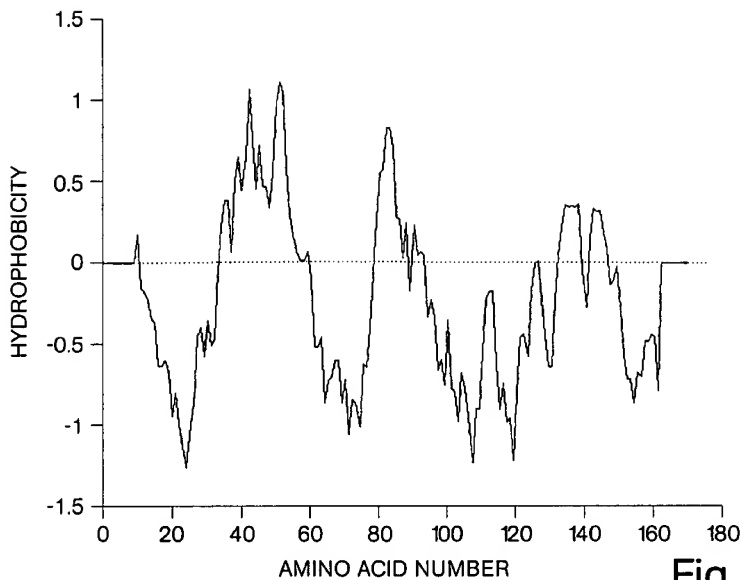


Fig. 22

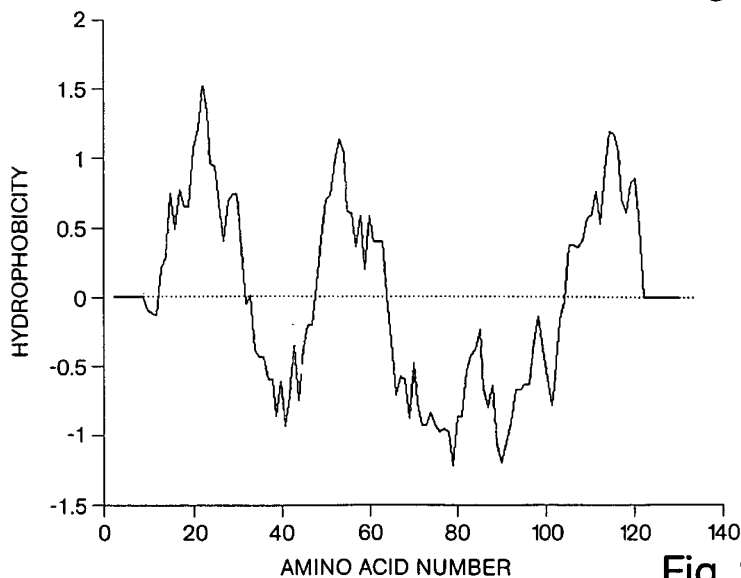


Fig. 23